METHODS OF TREATING ACNE AND ROSACEA WITH ELECTROCHEMICALLY GENERATED ZINC IONS

CROSS REFERENCE TO RELATED APPLICATIONS

This is a continuation-in-part of co-pending application Serial No. 10/609,727, filed on June 30, 2003, which is hereby incorporated by reference in its entirety.

FIELD OF THE INVENTION

The present invention relates to a device for application to a barrier membrane.

BACKGROUND OF THE INVENTION

Transdermal devices have been widely prescribed for decades in the treatment of is systemic diseases and local conditions. During passive transdermal delivery, an active agent is delivered into a mammal by using a concentration gradient across a barrier membrane (e.g., through passive diffusion through skin). For example, a patch containing the drug in high concentration is affixed to the skin of a patient.

Electricity may be employed to facilitate drug transport across the skin barrier. In electricity-assisted devices, an electric potential (voltage) is applied to the membrane to facilitate drug transport. In transdermal iontophoresis, an ionized drug migrates into the skin driven by an applied electric potential gradient. Anionic drugs are delivered into the skin under the cathode (negatively charged electrode), while cationic drugs are

delivered under the anode (positively charged electrode). Iontophoresis enables enhanced as well as better control of permeation rate of the ionic species into the skin.

The most common design of an iontophoresis device includes a power source (e.g., a battery), an electric control mechanism, and two separate conductive electrodes. Each conductive electrode is in contact with a separate electrolyte composition (with or without an active agent). The electrolyte or ionic active composition is generally either an aqueous solution contained in a liquid chamber or a semi-solid. The assembly of the conductive electrode and electrolyte composition is often referred to as "an electrode assembly" or simply "an electrode." The two electrode assemblies are usually affixed to the skin separated by electric insulation between them.

Alternatively, the two electrode assemblies may be constructed into a single iontophoresis device with an electric insulating material built between the two electrode assemblies for electrical isolation to prevent shorting current. An example of such an iontophoresis device is disclosed in U.S. Patent No. 5,387,189.

In another variation of the common iontophoresis device designs, the electrolyte composition in one of the two electrode assemblies is eliminated, and the conductive electrode is placed directly in contact with the skin to complete the electric circuit. An example of such iontophoresis device is disclosed in U.S. Patent No. 6,385,487.

During a typical iontophoresis operation (mono-polar operation), one of the two electrodes (i.e., active electrode) drives the active agent into the skin. The other electrode (i.e., disperse electrode) serves to close

the electrical circuit through the skin. Sometimes, a second active agent of opposite electric charge can be placed into electrolyte composition in contact with the second electrode, thus, being delivered into the skin under the second electrode. Alternatively, the electric polarity of the first and second electrodes can be reversed periodically to drive ionic species under both electrodes (bi-polar operation). A bi-polar iontophoresis device for transdermal drug delivery is disclosed U.S. Patent No. 4,406,658.

Acne and rosacea are major diseases of the skin associated with sebaceous follicles on the skin. There are many treatments, but no cures for acne or rosacea. Such treatments for acne include antibiotics (which kill or inhibit growth of *p. acnes* bacteria which play a role in acne), retinoids such as tretinoin and isotetinoin, antimicrobials such as benzoyl peroxide, and keratolytic agents such as salicylic acid. Rosacea can be treated with antibiotics, sulfur, sodium sulfacetamide, and retinoids. The present invention relates to a device that can be used to treat acne or rosacea, or other conditions that affect barrier membranes.

SUMMARY OF THE INVENTION

In one aspect, the present invention features a method of treating infections of the skin, including but not limited to, acne or rosacea, by applying to the skin electrochemically generated zinc ions. In one embodiment, the method includes topically applying a device including an anode containing zinc. In a further embodiment, the device includes a housing having a skin contacting surface; a first conductive electrode containing zinc; a

second conductive electrode; and a carrier; wherein the first conductive electrode is in electric communication with the second conductive electrode, wherein the first conductive electrode is in ionic communication with the carrier, and wherein the carrier is in communication with said skin contacting surface.

In another aspect, the present invention features a device having a barrier membrane contacting surface, the device containing: a power source; a first conductive electrode; a second conductive electrode; and a carrier; wherein the power source is in electric communication with the first conductive electrode and the second conductive electrode, wherein the first conductive electrode and the second conductive electrode are in ionic communication with the carrier, and wherein the carrier is in communication with the barrier membrane contacting surface. In another aspect, the present invention features a method of administering electricity to a human barrier membrane by applying to the membrane such a device. In another aspect, the present invention features a method of treating a skin condition by applying to the skin such a device.

In another aspect, the present invention features a device having a barrier membrane contacting surface, the device containing: a power source; a first conductive electrode; a second conductive electrode; and a carrier containing an active agent; wherein the power source is in electric communication with the first conductive electrode and the second conductive electrode, wherein the first conductive electrode and the second conductive electrode are in ionic communication with the carrier, and wherein the carrier is in communication with the barrier membrane

contacting surface. In another aspect, the present invention features a method of administering electricity to a human barrier membrane by applying to the membrane such a device. In another aspect, the present invention features a method of treating a skin condition by applying to the skin such a device.

In another aspect, the present invention features a device having a barrier membrane contacting surface, the device containing: a power source; a first conductive electrode; a second conductive electrode; a first light emitting diode; and a carrier containing an active agent; wherein the power source is in electric communication with the first conductive electrode, the second conductive electrode, and the light emitting diode, and wherein the device is arranged such that light from the first light emitting diode and the carrier are in communication with the barrier membrane contacting surface. In another aspect, the present invention features a method of administering an active agent to a human barrier membrane by applying to the membrane such a device. In another aspect, the present invention features a method of treating a skin condition by applying to the skin such a device.

In another aspect, the present invention features a method of treating a skin condition by applying to the skin a device having a barrier membrane contacting surface that administers an oxidizing agent to the barrier membrane, wherein the device contains: a power source; a first conductive electrode, wherein the first conductive electrode is an inert anode; a second conductive electrode, wherein the second conductive electrode is a cathode; and a carrier containing water; wherein the power

source is in electric communication with the first conductive electrode and the second conductive electrode, wherein the first conductive electrode is in ionic communication with the carrier, wherein the oxidizing agent is generated by electric current passing from the first conductive electrode through the carrier, and wherein the carrier is in communication with the barrier membrane contacting surface. In another aspect, the present invention features a method of administering an oxidizing agent to a barrier membrane by applying to the membrane such a device.

In another aspect, the present invention features a method of treating a skin condition by applying to the skin a device having a barrier membrane contacting surface that administers a reducing agent to the barrier membrane, wherein the device contains: a power source; a first conductive electrode, wherein the first conductive electrode is an inert cathode; a second conductive electrode, wherein the second conductive electrode is a anode; and a carrier containing water; wherein the power source is in electric communication with the first conductive electrode and the second conductive electrode, wherein the first conductive electrode is in ionic communication with the carrier, wherein the reducing agent is generated by electric current passing from the first conductive electrode through the carrier, and wherein the carrier is in communication with the barrier membrane contacting surface. In another aspect, the present invention features a method of administering an reducing agent to a barrier membrane by applying to the membrane such a device.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a cross-sectional view of one embodiment of the device suitable for practicing the invention. The battery 320 is located at the back of the device 500.

FIG. 2 is a cross-sectional view of one embodiment in accordance with the invention. The battery 320 is embedded in the carrier layer 120 of the device 500.

FIG. 3 is a cross-sectional view of one embodiment in accordance with the invention. The battery 320 is embedded in the carrier layer 120 that is enclosed in a chamber 160 with an opening affixed to the release liner 100 with an adhesive layer 130.

FIG. 4 is a top view of one embodiment in accordance with the invention showing the conductive electrodes 140 and 240 and carrier layer 120.

FIG. 5 is a top view of one embodiment in accordance with the invention showing the conductive electrodes 140 and 240 and carrier layer 120.

FIG. 6 is a cross-sectional view of one embodiment in accordance with the invention. The device 800 contains two electrode assemblies 200 and 600.

DETAILED DESCRIPTION OF THE INVENTION

It is believed that one skilled in the art can, based upon the description herein, utilize the present invention

to its fullest extent. The following specific embodiments are to be construed as merely illustrative, and not limitative of the remainder of the disclosure in any way whatsoever.

Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which the invention belongs. Also, all publications, patent applications, patents, and other references mentioned herein are incorporated by reference. Unless otherwise indicated, a percentage refers to a percentage by weight (i.e., %(W/W)).

What is meant by a "product" is a product containing the device in finished packaged form. In one embodiment, the product contains instructions directing the user to apply the device to the barrier membrane (e.g., to treat a skin condition). Such instructions may be printed on the device, label insert, or on any additional packaging.

In one aspect, the present invention features promoting a device of the present invention for its intended use. What is meant by "promoting" is promoting, advertising, or marketing. Examples of promoting include, but are not limited to, written, visual, or verbal statements made on the product or in stores, magazines, newspaper, radio, television, internet, and the like.

As used herein, "pharmaceutically-acceptable" means that the ingredients which the term describes are suitable for use in contact with the barrier membrane (e.g., the skin or mucosa) without undue toxicity, incompatibility, instability, irritation, allergic response, and the like.

As used herein, "safe and effective amount" means an amount of the ingredient or of the composition sufficient

to provide the desired benefit at a desired level, but low enough to avoid serious side effects. The safe and effective amount of the ingredient or composition will vary with the area being treated, the age and skin type of the end user, the duration and nature of the treatment, the specific ingredient or composition employed, the particular cosmetically-acceptable carrier utilized, and like factors.

As used herein, the term "treatment" means the treatment (e.g., alleviation or elimination of symptoms and/or cure) and/or prevention or inhibition of the condition (e.g., a skin condition). What is meant by a "skin condition" is a dermatological disease or disorder (including, but not limited, acne, rosacea, or skin infections) or skin characteristic (including, but not limited to, pigmentation, hair growth regulation, skin texture, skin firmness, skin elasticity, skin vasculature, dark circles, cellulite, sebum regulation, and skin shine). Examples of skin infections include, but are not limited to, those due to susceptible pathogens such as acne, rosacea, impetigo, folliculitis, furunculosis, ecthyma, eczema, psoriasis, atopic dermatitis, herpes, epidermolysis bullosa, icthyosis, and infected traumatic lesions (e.g., ulcers, minor burns, cuts, abrasions, lacerations, wounds, biopsy sites, surgical incisions and insect bites).

The present invention relates to a device for the delivery of electricity (e.g., to induce a desirable biological response) and/or an active agent into a barrier membrane. In one embodiment, the device of the present invention is a self-contained device containing a battery as power source and two conductive electrodes in electric

communication with the positive and negative poles of the battery. By "electric communication" is meant that electrons can pass between the elements of the device (e.g., between the power source and an conductive electrode of the device).

In one embodiment, the two conductive electrodes are in ionic communication with the carrier containing an electrolyte. By "ionic communication" it meant that ions of one or more electrolytes in the carrier are in contact with the conductive electrode. This electrode configuration differs from those in conventional iontophoresis devices in which each conductive electrode is in contact with a separate carrier (e.g., each electrode is contained in a separate compartment and affixed to the skin with electric insulation between them in order that all the electric current travels through the skin to complete the electric circuit). An advantage of such an embodiment of the present invention includes the capability of delivering simultaneously active agents of opposite charges from the same carrier into substantially the same skin site under the conductive electrodes.

The device contains a barrier membrane contacting surface (e.g., a skin contacting surface) that is applied to the membrane (e.g., applied by the user to the user's skin). The device is arranged such that carrier is in communication with the barrier membrane contacting surface (e.g., such that electricity and/or the active agent may be administered from the carrier into the barrier membrane). In one embodiment, the carrier is the barrier membrane contacting surface (e.g., the carrier is a hydrogel). In one embodiment, the device contains a light emitting diode such that light from the light emitting

diode is in communication with the barrier membrane contacting surface (e.g., such that the light may be administered to the barrier membrane).

In one embodiment, the device of the present invention delivers an active agent into the barrier membrane. The active agents to be delivered by the device of the present invention include active agents either initially incorporated in the carrier or electrochemically generated by the electric current passing from a conductive electrode through the carrier during use. What is meant by "electrochemically generated" is that the chemical specie is created as a result of an electrochemical reaction resulting from electric current flowing through an electrode, such a chemical specie released from a reactive electrode (e.g., an electrochemically generated zinc ion), a chemical specie electrochemically generated on the surface of an inert electrode, or a chemical specie that is a subsequent reaction product of such electrochemically generated specie.

Power Source

The power source may be conventional direct current (DC) or pulsed DC, such as that disclosed in U.S. Patent No. 5,042,975. In one embodiment, the current density to be used by the device in the present invention (current intensity per unit area of the barrier membrane) is generally less than about 0.5 mA/cm^2, such as less than about 0.1 mA/cm^2 or less than about 0.05 mA/cm^2. In one embodiment, the power source produces a voltage of from about 0.1 volts to about 9 volts, such as from about 1 to about 3 volts, such as about 1.5 volts.

In one embodiment, the power source is a battery (e.g., a rechargeable or disposable battery). In one embodiment, the battery is a disposable battery of small size suitable for a wearable patch or facial mask type adhesive device. Examples of suitable batteries include, but not limited to, button or coin batteries such as silver oxide, lithium, and zinc air batteries (which are typically used in small electronic devices). A zinc air battery is preferred because of its small size and high energy density, as well as its environmental friendliness. Examples of zinc air batteries include, but are not limited to, Energizer™ AC5 and AC10/230 (Eveready Battery Co. Inc., St. Louis, MO). Another preferred battery for the device is a flexible thin layer open liquid state electrochemical cell battery, such as a battery described in U.S. Patent No. 5,897,522.

In another embodiment, the power source is a galvanic couple, which is made of dissimilar materials, such as metal pairs, capable of acting as an electric source when brought in contact with an electrolyte. Examples of such galvanic couples include, but is not limited to, zinc-copper, zinc-silver, zinc-silver/silver chloride, aluminum-copper, aluminum-silver, aluminum-silver/silver chloride zinc-conductive carbon, copper-conductive carbon, and aluminum carbon. The materials which serve to make up the galvanic couple may also serve as the conductive electrodes of the device, e.g., zinc as the conductive anode and silver/silver chloride as the conductive cathode or zinc as the conductive anode and copper as the conductive cathode. In one embodiment, the materials that make up the galvanic couple have a standard potential

difference equal to or greater than about 0.1 volts, such as greater than about 0.5 volts.

Carrier

The carrier of the present invention is a liquid (e.g., a solution, a suspension, or an emulsion which may be immobilized within an absorbent material such as gauze or non-woven pad), a semi-solid (e.g., a gel, a cream, a lotion, microemulsion, or hydrogel), or a solid (e.g., a lyophilized composition containing active agents, which may be reconstituted by adding a liquid prior to use) that during use is capable of conducting electricity from a conducting electrode (e.g., the carrier contains one or more electrolytes, organic solvents, and water). In one embodiment, the carrier (e.g., a liquid or semi-solid) is added to the device by the user prior to applying the device to the barrier membrane.

Examples of electrolytes include, but are not limited to, pharmaceutically acceptable organic and organic salts and buffers. Examples of salts include, but are not limited to, chloride salts (such as sodium chloride, potassium chloride, lithium chloride, calcium chloride, strontium chloride, magnesium chloride or other chloride salts), as well as salts of sodium, potassium, lithium, calcium, magnesium, strontium, fluoride, iodide, bromide. Examples of buffers include, but are not limited to, phosphates, citrates, acetates, lactates, and borates.

In one embodiment, the electrolyte is an active agent, or becomes an active agent after the passage of the electric current through the carrier. Examples of such electrolyte-active agents include, but are not limited to,

salicylic acid, salicylates, and other weak acid or weak base active agents.

In one embodiment, the carrier contains water. In a further embodiment, the carrier may also contains one or more organic solvents. Examples of organic solvents include, but are not limited to: dimethyl isosorbide; isopropylmyristate; surfactants of cationic, anionic and nonionic nature; vegetable oils; mineral oils; waxes; gums; synthetic and natural gelling agents; alkanols; glycols; and polyols.

Examples of glycols include, but are not limited to, glycerin, propylene glycol, butylene glycol, pentalene glycol, hexylene glycol, polyethylene glycol, polypropylene glycol, diethylene glycol, triethylene glycol, glycerol, and hexanetriol, and copolymers or mixtures thereof. Examples of alkanols include, but are not limited to, those having from about 2 carbon atoms to about 12 carbon atoms (e.g., from about 2 carbon atoms to about 4 carbon atoms), such as isopropanol and ethanol. Examples of polyols include, but are not limited to, those having from about 2 carbon atoms to about 15 carbon atoms (e.g., from about 2 carbon atoms to about 10 carbon atoms) such as propylene glycol.

The organic solvents may be present in the carrier in an amount, based upon the total weight of the carrier, of from about 1 percent to about 90 percent (e.g., from about 5 percent to about 50 percent). Water may be present in the carrier (prior to use) in an amount, based upon the total weight of the carrier, of from about 5 percent to about 95 percent (e.g., from about 50 percent to about 90 percent).

The carrier may also contain: preservatives (such as cresol, chlorocresol, benzyl alcohol, methyl p-hydroxylbenzoate, propyl p-hydroxybenzoate, phenol, thimerosal, benzalkonium chloride, benzethonium chloride, and phenylmercuric nitrate); stabilizing agents or antioxidants (such as ascorbic acid, ascorbic acid esters, butylhydroxy anisole, butylhydroxy toluene, cysteine, N-acetylcysteine, sodium bisulfite, sodium metabisulfite, sodium formaldehydesulfoxylate, acetone sodium bisulfite, tocopherols, and nordihydroguaiaretic acid); chelating agents (such as ethylenediaminetetraacetic acid and its salts); buffers (such as acetic acid, citric acid, phosphoric acid, glutamic acid, and salts thereof); and tonicity adjusting agents (such as sodium chloride, sodium sulfate, dextrose and glycerin).

In one embodiment, the carrier may also contain a suspending material and/or a fluid-absorbing material (e.g., for physically stabilizing the ingredients of the carrier). Examples of suspending materials include, but are not limited to: cotton-based gauze; non-woven pads made of rayon or a mixture of rayon, polyester and/or other polymer fibers; open-cell foam and sponge-like materials contained of polyurethane, polyester and/or other polymers; and cross-linked and noncross-linked gelling materials, such as polyacrylamide, polyvinyl alcohol, gelatin, hydroxymethylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, methylcellulose, and carboxymethylcellulose.

Examples of fluid-absorbing materials include, but are not limited to: cross-linked and non-cross-linked polymers; swellable polymers such as water-swollen cellulose derivatives (e.g., methylcellulose (MC),

hydroxyethyl methylcellulose (HEMA), hydroxypropyl methylkcellulose (HPMC), ethylhydroxyethyl cellulose (EHEC), hydroxyethylcellulose (HEC), hydroxypropylcellulose (HPC), and carboxymethlcellulose (CMC) and their salts); polyvinyl alcohol (PVA); polyvinylpyrrolidone (PVP); polyethylene oxide (PEO); polymers prepared by monomers such as hydroxyethyl methacrylate (HEMA), hydroxyethoxyethyl emthacrylate (HEEMA), hydroxydiethoxyethl methacrylate (HDEEMA), methyoxyethyl methacrylate (MEMA), methoxyethoxyethyl methacrylate (MEEMA), methyldiethoxyethyl methacrylate (MDEEMA), ethylene glycol dimethacrylate (EGDMA), n-vinyl-2pyrrolidone (NVP), methacrylic acid (MA), and vinyl acetate (VAC); polycrylamide; gelatin; gums and polysaccharides such as gum arabic, gum karaya, gum tragacanth, guar gum, gum benzoin, and alginic acid and their salts; polyethylene glycol (PEG); polypropylene glycol (PPG); and clays or other swellable minerals such as bentonite and montmorillonite. The amount of fluid absorbable material in the carrier may range from about 0.1% to about 95%, by weight, such as from about 1% to about 20%, by weight, of the carrier.

Another embodiment of the present invention is directed to pairing one or more inert conductive electrodes in order to electrochemically generate oxidizing or reducing agents from electrochemically reactive materials in situ in the carrier. Such oxidizing or reducing agents can be used as active agents to treat barrier membrane conditions.

Examples of the electrochemically reactive materials in the carrier according to the present invention include, but are not limited to, water and compounds containing the

elements selected from the Periodic Table of the Elements VIB and VIIB (such as oxygen, sulfur, fluorine, chlorine, bromine, and iodine).

In one embodiment, the reactive material reacts with the inert anode to form an oxidizing agent. Examples of such a reactive material includes, but is not limited to, the ions OH^-, Cl^-, I^-, Br^-, SO_3^{2-}, and HCO_3^-. The present device, thus, enables to generation of oxidizing agents, such as nascent oxygen (e.g., singlet oxygen), chlorine and chlorine dioxide gases, which are difficult to formulate in a conventional topical product.

In one embodiment, the reactive material reacts with the inert cathode to form a reducing agent. Examples of such a reactive material includes, but is not limited to, oxidized or disulfide forms of thio-compounds with one or more sulfhydryl functional groups, thio-containing amino acids and their salts or esters, and sulfides. Examples of such thio-compounds include, but are not limited to: thioglycolic acid and its salts, such as thioglycolates of calcium, sodium, strontium, potassium, ammonium, lithium, magnesium, and other metal salts; thioethylene glycol; thioglycerol; thioethanol; thioactic acid; and thiosalicylic acid; and their salts. Examples of the thio-containing amino acids include, but are not limited to, L-cysteine, D-cysteine, DL-cysteine, N-acetyl-L- cysteine, DL-homocysteine, L-cysteine methyl ester, L-cysteine ethyl ester, N- carbamoyl cysteine, glutathione, and cysteamine. Examples of sulfides, include but are not limited to, calcium, sodium, potassium, lithium and strontium sulfides and glutathione disulfide. The inert cathode converts the aforementioned reactive oxidized or disulfide form of a sulfur-containing compound to a thio-containing compound,

or a sulfydryl-containing compound. Examples of such a conversion is the conversion of cystine to cysteine and the conversion of the oxidized form of glutathione to glutathione.

In one embodiment, the concentration of the reactive material in the carrier may range from about 0.01% to about 25%, by weight, such as from about 0.1% to about 10%, by weight, of the carrier. The pH value of the carrier may range from about pH 1.5 to about pH 9, preferably from pH 2 to pH 7, and most preferably from about pH 3 to pH 5.

In one embodiment, the carrier contains an adhesive. The adhesive is used to affix the device to the barrier membrane. Examples of hydrophobic adhesives include, but are not limited to, silicones, polyisobutylenes and derivatives thereof, acrylics, natural rubbers, and combinations thereof. Examples of silicone adhesives include, but are not limited to, Dow Corning 355 available from Dow Corning of Midland, MI; Dow Corningo X7-2920; Dow Corning X7-2960; and GE 6574 available from General Electric Company of Waterford, NY. Examples of acrylic adhesives include, but are not limited to, vinyl (D acetate-acrylate) multipolymers such as Gelva 7371, available from Monsanto Company of St. Louis, MO; Gelvao 7881; Gelva 2943; and 1-780 medical grade adhesive available from Avery Dennison of Painesville, OH. Examples of hydrophilic adhesives include, but are not limited to, gum papaya and other natural gums, MC, HEMA, HPMC, EHEC, HEC, HPC, CMC, PVA, PVP, PEO, HEMA, HEEMA, HDEEMA, MEMA, MEEMA, MDEEMA, EGDMA, NVP MA, VAC, polycrylamide. getatins, gum arabic, gum karaya, gum tragacanth, guar

gum, gum benzoin, and alginic acid and their salts, polyethylene glycol (PEG), and polypropylene glycol (PPG).

In one embodiment, the concentration of the adhesive in the carrier may range from about 0.1% to about 95%, by weight, such as from about 1% to about 20%, by weight, of the carrier.

Electrodes

The conductive electrodes of the present invention may be a reactive conductive electrodes or inert conductive electrodes. What is meant by a "reactive conductive electrode" is that the conductive electrode itself goes through a change in its chemical composition during the electrode chemical reactions occurring with the electric current passing through the electrode during the process. In one embodiment, the reactive conductive electrode is an anode made of reactive materials such as a pure metal or a metal alloy including, but not limited to, zinc, aluminum, copper, silver, titanium, tin, iron, and alloys thereof. Upon passage of an electric current, metal ions such as zinc, copper, and aluminum cations are released from the anode into the carrier and delivered into the barrier membrane. Such ions may serve therapeutic benefits such as anti-microbial effects, immulogic modulation, enzymatic regulation, and/or anti-inflammatory effects.

In one embodiment, zinc ions are electrochemically generated by a zinc anode in, or are subsequently added to, a topical composition. The topical composition is then applied to the barrier membrane of the user for the intended beneficial effects from the zinc ions and other active agents present in the topical composition. The

active agents in the topical composition may contain anti-acne agents such as salicylic acid or benzoyl peroxide. One method of producing such electrochemically generated zinc ions is to incorporate an electrochemical device for zinc generation into a packaging and/or dispensing container of the topical composition (e.g., bottle equipped with a dispensing pump for an acne-treating/-preventing skin cream). In one embodiment, an electrochemical device including a zinc anode, a silver/silver chloride cathode, and a power source (e.g., a battery) electrically communicating with each other, is included within the dispensing pump. As the topical composition (such as a cream) passes out of the dispensing pump, it comes into contact with both the zinc anode and cathode and completes the electric circuit (i.e., an electric current runs from the anode into the cream, and returns to the power source via the cathode), the zinc anode begins to release zinc ions into the cream. Alternatively, the electrochemical device for zinc generation does not contain a battery. Instead, the zinc anode and cathode are connected to form a galvanic couple to generate zinc ions when both electrodes come into contact with the cream.

In one embodiment, the reactive conductive electrode is made of reactive materials such as metal halides (e.g., silver-silver chloride (Ag/AgCl), silver-silver bromide, and silver-silver iodide). In this case, the primary electrochemical reaction at the cathode surface is conversion of solid silver halide to metallic silver with little unwanted consumption of the oxidizing agents generated by the anode. The released halide ions may be subsequently oxidized to oxidizing agents, such as

chloride ions to chlorine (Cl_2), hypochlorous acid (HClO), and hypochlorite ions (ClO^-), and iodide ions to iodine.

What is meant by an "inert conductive electrode" is that the conductive electrode itself does not go through a change in its chemical composition. In one embodiment, the anode is made of an inert conductive electrode, so that the electrochemical process at the surface of the anode generates oxidizing agents such as nascent oxygen (e.g., by electrolysis of water) and/or chlorine-containing oxidizing agents such as chlorine, hypochlorite, chlorate and perchlorate, and chlorine dioxide. Nascent oxygen is an oxidizing agent that is inhibitive to P. acnes, and chlorine-containing oxidizing agents are potent antimicrobial agent with bacteriacidal activity.

In one embodiment, the inert conductive electrode is made of, or coated on the surface with, an inert materials such as noble metals (e.g., gold, platinum, or gold-coated conductive metals), conductive carbon (e.g., glassy carbon or graphite), carbon-embedded polymers (e.g., carbon silicone rubbers), conductive carbon polymer foam or sponge, silver halide-coated silver (e.g., silver chloride-coated silver, silver bromide-coated silver, and silver iodide-coated silver), and corrosive resistant alloys.

In one embodiment, the ratio of the conductivity measured between the first conductive and second conductive electrode of (i) the carrier and (ii) the skin hydrated with such carrier (wherein substantially all of the current passes between the electrodes through the skin) is in a range from about 10000:1 to about 1:100. In other words, the electric current distribution between

$I_{carrier}$ (the current passing through the carrier) and I_{skin} (the current passing through the skin) is such that the value of $I_{carrier}$ / I_{skin} is between about 10,000 and about 0.01.

Decreasing the ratio of the conductivity of the carrier to the conductivity of the skin will result in a greater percentage of current passage through the skin, thereby enhancing iontophoretic delivery of any active agents being so delivered into the skin. Decreasing the conductivity of the carrier can nonexclusively be accomplished by adding less conductive materials to the carrier. Examples of such less conductive materials include, but are not limited to, oils such as silicone or hydrocarbon oils, air pockets such as air bubbles or air pockets in a semi-solid carrier, or polymer or clay beads. In one embodiment where the primary intention is to electrochemically generate species in the carrier, the value of $I_{carrier}$ / I_{skin} is between about 10,000 and about 1. In another embodiment where the primary intention is to deliver electricity and/or active agents into the skin, the value of $I_{carrier}$ / I_{skin} is between about 10 and about 0.01.

Active Agents

In one embodiment, the carrier contains one or more active agents. What is meant by an "active agent" is a compound (e.g., a synthetic compound or a compound isolated from a natural source) that has a cosmetic or therapeutic effect on the barrier membrane.

In one embodiment, the carrier contains an anti-acne and/or anti-rosacea agent. Examples of anti-acne and anti-rosacea agents include, but are not limited to:

retinoids such as tretinoin, isotretinoin, motretinide, adapalene, tazarotene, azelaic acid, and retinol; salicylic acid; benzoyl peroxide; resorcinol; sulfur; sulfacetamide; urea; antibiotics such as tetracycline, metronidazole, and erythromycin; anti-inflammatory agents such as corticosteroids (e.g., hydrocortisone), ibuprofen, naproxen, and hetprofen; and imidazoles such as ketoconazole and elubiol; and salts, esters, and other derivatives thereof. Other examples of anti-acne active agents include essential oils, alpha-bisabolol, dipotassium glycyrrhizinate, camphor, β-glucan, allantoin, feverfew, flavonoids such as soy isoflavones, saw palmetto, chelating agents such as EDTA, lipase inhibitors such as silver and copper ions, hydrolyzed vegetable proteins, inorganic ions of chloride, iodide, fluoride, and their nonionic derivatives chlorine, iodine, fluorine, and other valences, synthetic phospholipids and natural phospholipids such as Arlasilk™ phospholipids CDM, SV, EFA, PLN, and GLA (Uniqema, ICI Group of Companies, Wilton, UK).

In one embodiment, the device of the present invention contains an anti-aging agent. Examples of suitable anti-aging agents include, but are not limited to: inorganic sunscreens such as titanium dioxide and zinc oxide; organic sunscreens such as octyl-methoxy cinnamates; retinoids; vitamins such as vitamin E, vitamin A, vitamin C, and vitamin B and vitamin salts or derivatives such as ascorbic acid di-glucoside and vitamin E acetate or palmitate; alpha hydroxy acids such as glycolic acid, citric acid, lactic acid, malic acid, mandelic acid, ascorbic acid, alpha-hydroxybutyric acid, alpha- hydroxyisobutyric acid, alpha-hydroxyisocaproic

acid, atrrolactic acid, alpha-hydroxyisovaleric acid, ethyl pyruvate, galacturonic acid, glucoheptonic acid, glucoheptono 1,4-lactone, gluconic acid, gluconolactone, glucuronic acid, glucuronolactone, isopropyl pyruvate, methyl pyruvate, mucic acid, pyruvic acid, saccharic acid, saccaric acid 1,4-lactone, tartaric acid, and tartronic acid; beta hydroxy acids such as beta-hydroxybutyric acid, beta-phenyl-lactic acid, and beta-phenylpyruvic acid; zinc and zinc containing compounds such as zinc oxides; and botanical extracts such as green tea, soy, milk thistle, algae, aloe, angelica, bitter orange, coffee, goldthread, grapefruit, hoellen, honeysuckle, Job's tears, lithospermum, mulberry, peony, puerarua, nice, and safflower; and salts, esters, and other derivatives thereof.

In one embodiment, the carrier contains a depigmentation agent. Examples of suitable depigmentation agents include, but are not limited to: soy extract; soy isoflavones; retinoids such as retinol; kojic acid; kojic dipalmitate; hydroquinone; arbutin; transexamic acid; vitamins such as niacin and vitamin C; azelaic acid; linolenic acid and linoleic acid; placertia; licorice; and extracts such as chamomile and green tea; and salts, esters, and other derivatives thereof.

In one embodiment, the carrier contains a plant extract. Examples of plant extracts include, but are not limited to, feverfew, soy, glycine soja, oatmeal, what, aloe vera, cranberry,hazel witch, alnus, arnica, artemisia capillaris, asiasarum root, birch, calendula, chamomile, cnidium, comfrey, fennel, galla rhois, hawthorn, houttuynia, hypericum, jujube, kiwi, licorice, magnolia, olive, peppermint, philodendron, salvia, sasa albo-

marginata, natural or synthetic isoflavonoids, soy isoflavones, natural or synthetic essential oils.

In one embodiment, the carrier contains metals such as metal ions, metal salts, metal complexes, fine metal powders, fine metal coated fibers and fabrics of synthetic or natural origin, or fine metal fibers. Examples of such metals include, but are not limited to, zinc, copper, aluminum, gold, silver, titanium. The metal ions provide benefits such as antimicrobial, anti-inflammatory, and/or sebum-reduction effects. The beneficial metal ions may be released from the metal anode as the result of an electrochemical oxidation reaction concurrent with electric current passage (e.g., zinc ions electrochemically generated from a zinc anode).

In another embodiment, the beneficial ions may be generated indirectly from the electrochemical reactions at the electrode surface, such as the generation of hydrogen or hydroxyl ions at an inert electrode, which subsequently leads to a process to generate beneficial ions. For example, a device of the present invention may contain a power source, an inert anode (e.g., platinum, platinum coated conductive electrode, gold, or gold-coated conductive electrode), a reactive cathode (e.g., silver/silver chloride electrode), and an aqueous carrier composition containing an oxide (e.g., zinc oxide particles) among other active agents. During application to the skin, the electrolysis of water at the inert anode produces excess hydrogen ions which acidify the carrier toward a lower pH value, while the electrochemical reaction at the reactive cathode (e.g., the conversion of silver chloride to silver ions) does not affectthe pH. As the solution becomes more acidic, the oxide starts to

dissolve to release ions (e.g., zinc ions) for their beneficial effects to the barrier membrane.

Other active agents include those commonly used as for topical treatment and in cosmetic treatment of skin tissues, such as topical antibiotics for wounds, topical antifungal drugs to treat fungal infections of the skin and nails, and antipsoriatic drugs to treat psoriatic lesions of the skin and psoriatic nails.

Examples of antifungal drugs include but are not limited to miconazole, econazole, ketoconazole, sertaconazole, itraconazole, fluconazole, voriconazole, clioquinol, bifoconazole, terconazole, butoconazole, tioconazole, oxiconazole, sulconazole, saperconazole, clotrimazole, undecylenic acid, haloprogin, butenafine, tolnaftate, nystatin, ciclopirox olamine, terbinafine, amorolfine, naftifine, elubiol, griseofulvin, and their pharmaceutically acceptable salts. In one embodiment, the antifungal drugs are an azole, an allylamine, or a mixture thereof.

Examples of antibiotics (or antiseptics) include but are not limited to mupirocin, neomycin sulfate bacitracin, polymyxin B, 1-ofloxacin, tetracyclines (chlortetracycline hydrochloride, oxytetracycline - 10 hydrochloride and tetrachcycline hydrochoride), clindamycin phsphate, gentamicin sulfate, metronidazole, hexylresorcinol, methylbenzethonium chloride, phenol, quaternary ammonium compounds, tea tree oil, and their pharmaceutically acceptable salts.

Examples of antimicrobials include but are not limited to salts of chlorhexidine, such as lodopropynyl butylcarbamate, diazolidinyl urea, chlorhexidene digluconate, chlorhexidene acetate, chlorhexidene

isethionate, and chlorhexidene hydrochloride. Other cationic antimicrobials may also be used, such as benzalkonium chloride, benzethonium chloride, triclocarbon, polyhexamethylene biguanide, cetylpyridium chloride, methyl and benzothonium chloride. Other antimicrobials include, but are not limited to: halogenated phenolic compounds, such as 2,4,4',-trichloro-2- hydroxy diphenyl ether (Triclosan); parachlorometa xylenol (PCMX); and short chain alcohols, such as ethanol, propanol, and the like. In one embodiment, the alcohol is preferably at a low concentration (e.g., less than about 10% by weight of the carrier, such as less than 5% by weight of the carrier) so that it does not cause undue drying of the barrier membrane.

Examples of antipsoriatic drugs or drugs for seborrheic dermatitis treatment include, but are not limited to, corticosteroids (e.g., betamethasone dipropionate, betamethasone valerate, clobetasol propionate, diflorasone diacetate, halobetasol propionate, triamcinonide, dexamethasone, fluocinonide, fluocinolone acetonide, halcinonide, triamcinolone acetate, hydrocortisone, hydrocortisone verlerate, hydrocortisone butyrate, aclometasone dipropionte, flurandrenolide, mometasone furoate, methylprednisolone acetate), methotrexate, cyclosporine, calcipotriene, anthraline, shale oil and derivatives thereof, elubiol, ketoconazole, coal tar, salicylic acid, zinc pyrithione, selenium sulfide, hydrocortisone, sulfur, menthol, and pramoxine hydrochloride, and salts, esters, and other derivatives thereof. Examples of anti-viral agent, include, but are not limited to, imiquimod and its derivatives, podofilox,

podophyllin, interferon alpha, acyclovir, famcyclovir, valcyclovir, reticulos and cidofovir.

Examples of anti-inflammatory agent, include, but are not limited to, suitable steroidal anti-inflammatory agents such as corticosteroids such as hydrocortisone, hydroxyltriamcinolone alphamethyl dexamethasone, dexamethasone-phosphate, beclomethasone dipropionate, clobetasol valerate, desonide, desoxymethasone, desoxycorticosterone acetate, dexamethasone, dichlorisone, diflorasone diacetate, diflucortolone valerate, fluadrenolone, fluclarolone acetonide, fludrocortisone, flumethasone pivalate, fluosinolone acetonide, fluocinonide, flucortine butylester, fluocortolone, fluprednidene (fluprednylidene)acetate, flurandrenolone, halcinonide, hydrocortisone acetate, hydrocortisone butyrate, methylprednisolone, triamcinolone acetonide, cortisone, cortodoxone, flucetonide, fludrocortisone, difluorosone diacetate, fluradrenalone acetonide, medrysone, amciafel, amcinafide, betamethasone and the balance of its esters, chlorprednisone, chlorprednisone acetate, clocortelone, clescinolone, dichlorisone, difluprednate, flucloronide, flunisolide, fluoromethalone, fluperolone, fluprednisolone, hydrocortisone valerate, hydrocortisone cyclopentylproprionate, hydrocortamate, meprednisone, paramethasone, prednisolone, prednisone, beclomethasone dipropionate, betamethasone dipropionate, and triamcinolone. The preferred steroidal anti-inflammatory for use in the present invention is hydrocortisone. A second class of anti-inflammatory agents which is useful in the compositions of the present invention includes the nonsteroidal anti-inflammatory agents.

Other active agents include, but are not limited to, wound healing enhancing agent, scar reducing agents, analgesic agents, anesthetics, hair growth enhancing agents such as minoxadil, antihypertensives, drugs to treat coronary artery diseases, anticancer agents, endocrine and metabolic medication, neurologic medications, medication for cessation of chemical additions, motion sickness, and protein and peptide drugs.

In one embodiment, the carrier contains a fragrance effective for reducing stress, calming, and/or affecting sleep such as lavender and chamomile.

The amount of the active agent in the carrier will depend on the active agent and/or the intended use of the device. In one embodiment, the carrier contains a safe and effective amount of the active agent, for example, from about 0.001 percent to about 20 percent, by weight,, such as from about 0.01 percent to about 5 percent, by weight, of the carrier.

Light Emitting Diode

In one embodiment, the device contains one or more light emitting diodes. Light emitting diodes (LEDs) of certain spectrum may be incorporated into the device to emit light to the barrier membrane (e.g., to treat skin conditions such as acne and rosacea). The light emitting diode may also provide a signal to the user indicating that the device is operating properly.

In one embodiment, the LED is one that emits light periodically (i.e., a blinking LED). In a further embodiment, such LED also modulates the current passing through the barrier membrane to form a pulsatile DC current. Such pulsatile DC current can enhance delivery of

active agents into the barrier membrane, stimulate biological responses in the barrier membrane such as enhancing wound healing (e.g., in acne lesions), and/or enhanced skin sensation which serves a signal to a user that the device is working. Another potential advantage of using a blinking LED is to produce pulsatile DC current without the need of a complex electric circuit.

The spectrum of the LED's according to the current invention may range from about 300 nm to about 1500 nm, such as from about 350 nm to about 1000 nm. In one embodiment, the range of the LED includes violet-blue, green, red, and infrared ranges, e.g., from about 400 nm to about 450 nm such as from about 407 nm to about 420 nm; from about 510 nm to about 550 nm; from about 600 nm to about 700 nm; and from about 1300 nm to about 1500 nm. In one embodiment, the device contains two LEDs, one that emits light having a wavelength of from about 400 nm to about 500 nm and one which emits light from about 700 nm to about 1000 nm.

Photosensitizer agents, such as 5-aminolaevulinic acid (ALA), hypericin, St. John's wort powder or extract, or other synthetic or natural photosensitizer agents, may be incorporated into the carrier as active agents to be delivered and irradiated by the device with LED's of the present invention. The light irradiation from the LED's, together with the photosensitizer agent(s) and other aforementioned active agents, electrochemically generated oxidizing agents (e.g., peroxides, nascent oxygen, chlorine dioxide, and chlorine), and/or electric stimulation of the barrier membrane may work synergistically to achieve an improved efficacy in treating membrane disorders such as acne and rosacea.

Use

In one embodiment, the device is used for the treatment of a barrier membrane condition (e.g., the delivery of an active agent, light, and/or electricity into the membrane such as the skin, vaginal, or rectal mucosa barrier membrane of a human). In one embodiment, the device is used for the treatment of skin conditions. Examples of such treatments include, but are not limited to: treatment of acne, rosacea, or other microbial infections of the skin; reduction the visible signs of skin aging (e.g., wrinkles, sagging, and age-spots); folliculitis and pseudo-folliculitis barbae; treatment of wounds and lesions (e.g., enhancing healing and scar reduction); sebum regulations (e.g., sebum reduction or oily/shining skin appearance inhibition or control); pigmentation regulation (e.g., reduction of hyperpigmentation or pigmentation of light skin); hair growth retardation (e.g., skin on the leg) or hair stimulation (e.g., scalp); and treatment of dermatitis (e.g., atopic, contact, or seborrheic dermatitis) and/or psoriasis.

In another embodiment, the device is used for the treatment of mucosal conditions (e.g., mucosa in the oral or vaginal cavities). Examples of such treatments include, but are not limited to: treatment of vaginal candidiasis and vaginosis, genital and oral herpes, cold sore, canker sore, oral hygiene, periodontal disease, and other microbial infections of the mucosa.

Another embodiment of the present invention is the device induces certain desirable biological responses that facilitate the treatment of the barrier membrane

conditions. These desirable biological responses may be induced by the electric current passage through the barrier membrane, and/or the electrochemically generated oxidizing materials, together with the active agents delivered by iontophoresis from the carrier, in treating the barrier conditions. Examples of the desirable responses of the barrier membrane may include, but are not limited to, sebum regulation (e.g., reduction of sebaceous gland activity), inhibition of anaerobotic microbial growth and establishment of a healthier membrane microflora or (e.g, reduction of P. acne growth and of production of irritating fatty acids), blood vasoconstriction (thus promoting local accumulation of active agents or removal of dark circle under the eye due to deoxyhemoglobins), enhanced tissue immunological activity (e.g, increased elimination of pathogenic microbes on tissue's own defense systems), improved tissue repairing (e.g., enhanced healing and reduced scarring of lesions such as acne lesions), and improved keratolytic activity of the carrier (e.g., softening of keratin plugs of comedos in whiteheads and blackheads of acne, and facilitating their removal).

In another aspect, the invention also features the method of converting an active agent from a less active form to a more active form via oxidation or reduction via an inert electrode (e.g., cystine to cysteine, disulfide acetyl-cysteine to acetyl-cysteine, and retinol to retinoic acid). Thus, an unstable agent can be stored in a more stable form and converted to its active form prior to administration. In a further aspect, the generation of reducing agents by the device of the present invention can be used to stabilize oxygen-labile active agents.

Examples of such oxygen-labile active agents include, but are not limited to, retinoids, ascorbic acid, and benzoyl peroxide.

In one embodiment, the invention also features the method of converting an active agent from a less active form to a more active form via oxidation at an reactive anode, such as an anode made of zinc, copper, or aluminum. For example, an anode made of zinc releases zinc ions with the passage of an electric current through the electrode. The zinc ions generated by such an electrochemical reactions are then subsequently delivered by the electric repulsion of the positively charged anode into the barrier membrane. In one embodiment, such ions aredeposited into the hair follicles and/or sebaceous glands to inhibit *P. acnes* growth and/or suppress skin tissue inflammation resulted from *P. acnes* over growth before the treatment.

Shape

The device includes a housing that may be fabricated into various shapes and sizes to fit the contours of various anatomical surfaces of the barrier membranes. For examples, the housing may be a substrate made in the shape of a whole facial mask with openings/holes to expose the eyes, eye bows, nose, and mouth; a partial facial mask covering only the upper or lower half of the face; or a patch covering only the forehead, or the under eye region, the chin and jaw region, the neck, the back, wound, acne lesion or pimple, or other specific area of a barrier membrane in need of treatment.

In one embodiment of the present invention, the housing is a water-insoluble substrate containing a galvanic couple, for example, a fine zinc wire or a fine zinc-

coated fiber (e.g., zinc-coated polymer fiber) connected to a fine copper wire or a fine copper-coated fiber (e.g., copper-coated polymer fiber). One or more such fine galvanic couple wire(s) or fiber(s) may be incorporated into the substrate to create a device which, when in contact with the carrier (such as tap water or a liquid or semi-liquid composition including active agents) generates an electric current. In one embodiment, a galvanic couple-containing substrate may be made of multiple layer, for example, a layer of the zinc-containing substrate (e.g., a fine zinc wire- or a fine zinc-coated fiber in a woven or non-woven fabric) over a layer of copper-containing substrate (e.g., a fine copper wire- or a fine copper-coated fiber in a woven or non-woven fabric). During use, the layers contact each other to form the galvanic couple. In a further embodiment, the device releases beneficial ions (e.g., zinc ions or aluminum ions) that are delivered to the barrier membrane (e.g., the skin) when such a substrate is applied by the user (e.g., used as a wipe for cleaning the skin or a facial patch or mask to treat the skin). Active agents may also be incorporated into the substrate during manufacturing processes or be subsequently applied to the substarte prior to the application to the barrier membrane (e.g., in the form of an electrolyte or active agent containing liquid spray to wet the substrate). In one embodiment, the fabric is used as a dry wipe or a dry full or partial facial mask, to be wetted immediately before use, by applying water to the dry wipe or facial mask to pre-moisturized skin (e.g., by washing with tap water).

By "water insoluble" is meant that the substrate, upon immersion in distilled water at 25°C, does not

readily dissolve in or readily break apart. The water-insoluble substrate may, however, be disintegrated and/or dissolved slowly, i.e., over a period of several hours up to several days. A wide variety of materials can be used as the water-insoluble substrate. Examples of suitable substrates include, but are not limited to, non-woven substrates, woven substrates, hydro-entangled substrates, air entangled substrates, natural sponges, synthetic sponges, and polymeric netted meshes.

The water insoluble substrates may be flushable. As used herein, by "flushable" is meant that the substrate will pass through at least 10 feet of waste pipe in two toilet flushes. The material may also be biodegradable.

In one embodiment, the substrates contain a non-woven material. By "non-woven" is meant that the substrate, or a layer of the substrate, is comprised of fibers that are not woven into a fabric but rather are formed into a sheet, mat, or pad layer. The fibers can either be random (i.e., randomly aligned) or they can be carded (i.e., combed to be oriented in primarily one direction. Furthermore, the non-woven substrate can be composed of a combination of layers of random and carded fibers).

Non-woven substrates may be comprised of a variety of natural and/or synthetic materials. By "natural" is meant that the materials are derived from plants, animals, insects, or byproducts of plants, animals, and insects. By "synthetic" is meant that the materials are obtained primarily from various man-made materials or from natural materials, which have been further altered.
Non-limiting examples of natural materials useful in the present invention are silk fibers, keratin fibers (such as wool fibers, camel hair fibers) and cellulosic fibers

(such as wood pulp fibers, cotton fibers, hemp fibers, jute fibers, and flax fibers).

Examples of synthetic materials include, but are not limited to, those selected from the group containing acetate fibers, acrylic fibers, cellulose ester fibers, cotton fibers, modacrylic fibers, polyamide fibers, polyester fibers, polyolefin fibers, polyvinyl alcohol fibers, rayon fibers, polyurethane foam, and mixtures thereof.

Substrates made from one ore more of the natural and synthetic materials useful in the present invention can be obtained from a wide variety of commercial sources such as Freudenberg & Co. (Durham, NC USA), BBA Nonwovens (Nashville, TN USA), PGI Nonwovens (North Charleston, SC USA), Buckeye Technologies/Walkisoft (Memphis, TN USA), and Fort James Corporation(Deerfield, IL USA).

Methods of making non-woven substrates are also well known in the art. Such methods include, but are not limited to, air-laying, water-laying, melt-blowing, spin-bonding, or carding processes. The resulting substrate, regardless of its method of production or composition, is then subjected to at least one of several types of bonding operations to anchor the individual fibers together to form a self-sustaining web. The non-woven substrate can be prepared by a variety of processes including hydro-entanglement, thermally bonding, and combinations of these processes. Moreover, the substrates can have a single layer or multiple layers. In addition, a multi-layered substrate can include film layer(s) (e.g., aperture or non-aperture film layers) and other non-fibrous materials.

Strength or firmness of the non-woven material may be a desirable attribute. This can be achieved, for example,

by the addition of binding materials, such as wet strength resins, or the material may be made of polymer binder coatings, stable fibres, e.g. based on cotton, wool, linen and the like. Examples of wet strength resins include, but are not limited to, vinyl acetate-ethylene (VAE) and ethylene-vinyl chloride (EVCL) Airflex emulsions (Air Products, Lehigh, PA), Flexbond acrylic polymers (Air Products, Lehigh, PA), Rhoplex ST-954 acrylic binder (Rohm and Haas, Philadelphia, PA), and Ethylene-vinyl acetate (EVA) emulsion (DUR-O-SET® by National Starch Chemicals, Bridgewater, NJ). The amount of binding material in the substrate may range from about 5% to about 20%, by weight, of the substrate.

Non-woven materials of increased strength can also be obtained by using the so-called spunlace or hydro-entanglement technique. In this technique, the individual fibers are twisted together so that an acceptable strength or firmness is obtained without the need to use binding materials. The advantage of the latter technique is the excellent softness of the non-woven material.

In one embodiment, the non-woven material is made of a superabsorbent polymer. For the purposes of the present invention, the term "superabsorbent polymer" refers to materials which are capable of absorbing and retaining at least about 10 times their weight in body fluids under a 0.5 psi pressure. The superabsorbent polymer particles of the invention may be inorganic or organic crosslinked hydrophilic polymers, such as polyvinyl alcohols, polyethylene oxides, crosslinked starches, guar gum, xanthan gum, and other material known to the art of absorbent article manufacture.

Additives may also be added in order to increase the softness of the substrates. Examples of such additives include, but are not limited to, polyols such as glycerol, propylene glycol and polyethylene glycol, phthalate derivatives, citric esters, surfactants such as polyoxyethylene (20) sorbitan esters, and acetylated monoglycerides.

Sensory attributes may also be incorporated to the insoluble non-woven substrates. Examples of such sensory attributes include, but are not limited to color, texture, pattern, and embossing.

In one embodiment, the device of the present invention is for use as a wipe or towel (for example, having a surface area of from about 20 cm^2 to about 10,000 cm^2). In another embodiment, the device of the present invention is for use as a therapeutic patch or mask for application to a portion of or substancially all of the face (for example, having a surface area of from about 1 cm^2 to about 600 cm^2)

In one embodiment, the carrier is present in at least about 50%, such as at least about 75%, by weight of the total weight of the water insoluble substrate prior to use. In another embodiment, (i) the liquid carrier is present in less than about 10%, such as less than about 1%, by weight of the total weight of the water insoluble substrate (for example, the device may not contain any carrier prior to use). In a further embodiment, the product contains instructions for the user to either (i) wet the substrate prior to application or (ii) wet the barrier membrane (e.g., the skin) with water and/or another liquid prior to application.

Devices

One embodiment of the present invention is represented schematically in FIG. **1**. The device **500** contains a removable release liner **100**, a carrier layer **120**, a first conductive electrode **140**, a second conductive electrode **240**, electric lead wires **110** and **210** connecting the two poles of a battery **320** to the two oppositely charged conductive electrodes, an electric power switch **330** located on the lead wire **220**, a light emitting diode (LED) **122**, a backing layer **160** separating the carrier layer **120** from the battery **320**, and a battery cover layer **340**.

The gap "*b*" depicts the distance between two conductive electrodes **140** and **240** to the release liner (or the membrane following application of the device), and the gap "*a*" represents the distance between two oppositely charged conductive electrodes. In one embodiment, the ratio of gap "*a*" to gap "*b*" is at least about 1, such as at least about 2 or at least about 5.

The backing layer **160** may be impermeable to the active agent contained within the carrier layer **120**, and is preferably not permeable to water or other solvents in the carrier layer **120**. The battery **320** may be encased in an electric insulating, water-impermeable polymer layer (not shown in the figure). The backing layer **160** and the batter cover layer **340** may be made of flexible material that is impermeable to water, e.g., polymers such as polyethylene, polypropylene, polyvinyl acetate, polyurethane, silicone rubber, or polyvinyl chloride.

Optionally, there can be an electric circuit (not shown) in device **500** to provide a constant current located

between the battery **320** and conductive electrode **140** and/or conductive electrode **240**.

In a further embodiment, the backing layer **160** is permeable to electrochemically generated gases (e.g., oxygen, chlorine, and hydrogen) in order to limit excess accumulation of the gases in the carrier which can cause tissue irritation and/or undesirable deformation of the device.

The carrier layer **120** is an adhesive hydrogel containing the active agent. The active agent may be incorporated into the carrier layer **120** as dissolved molecules and ions, dispersed solid particles, or liquid droplets such as cream, lotion, emulsion, multi-emulsion, microemulsion, and/or liposome compositions. The carrier layer **120** may also contain a solid supporting matrix (e.g., a gauze, non-woven or sponge-like material).

A removable liner sheet **100** covers the carrier layer **120**. The selection of the removable release-liner **100** is dependent on the type of the adhesive hydrogel used in carrier layer **120**. The release liner sheet **100** is typically a polymer sheet or a paper or fabric coated with a polymer, which has weak adhesion toward the adhesive hydrogel layer **120**, thereby allowing it to be easily removed from the carrier layer **120** prior to use without damaging the carrier layer **120**. Examples of the polymers typically used for the release liner **100** are silicones and polyethylenes. Alternatively, a wax may be used in the place of the polymer to coat the release liner **100**.

In addition to, or in lieu of, the use of an adhesive in the carrier layer **120**, the device **500** may be fastened to the barrier membrane with an adhesive tape, an elastic

band, a band with a buckle (similar to a leather watch band), or a Velcro® band.

In order to use device **500**, the removable release liner sheet **100** is peeled off, and the carrier hydrogel layer **120** of the device **500** is affixed to a barrier membrane, such as the skin, vaginal, or rectal mucosa barrier membrane, of the user. The device may be directly affixed to the barrier membrane if the carrier layer **120** contains an adhesive hydrogel. An electric potential is applied across the conductive electrodes **140** and **240** by switching on the power switch **330**. Another embodiment of the present invention is represented schematically in FIG. 2. The battery **320** is located within the carrier layer **120.** The advantage of this battery arrangement includes reduced bulkiness, enhanced esthetics and user comfort.

Another embodiment of the present invention is represented schematically in FIG. 3. Housing **170** contains an adhesive layer **130** coated onto the rim of the housing **170** for affixing device **500** to membrane during application. The housing **170** may be made of the same materials as the backing layer **160** described above. The adhesive in the adhesive layer **130** may be a polymeric, pressure sensitive and/or nonconductive. Suitable adhesive materials include, but are not limited to, silicones, polyisobutylenes and derivatives thereof, acrylics, natural rubbers, and combinations thereof. Suitable silicone adhesives include, but are not limited to, Dow Corning 355 (available from Dow Corning of Midland, MI); Dow Corning X7-2920; Dow Corning 0 X7-2960; GE 6574 (available from General Electric Company of Waterford, NY); and silicone pressure sensitive adhesives. Suitable acrylic adhesives include, but are not limited to, vinyl

acetate-acrylate multipolymers, including, such as Gelva-7371 (available from Monsanto Company of St. Louis, MO); Gelva T 7881; Gelvac 2943; 1-780 medical grade adhesive available from Avery Dennison of Painesville, OH; and acrylic pressure sensitive adhesives.

When a zinc air battery is used as the power source of the device **500**, the battery **320** is constructed in such a way that the orifice on the stainless steel cover is facing the opposite side of the carrier layer **120**. An orifice is made on the battery cover layer to expose the orifice on the zinc air battery that is covered by a removable oxygen-impermeable cover. In this case, the power switch **230** is replaced by the removable oxygen-impermeable cover. The removable oxygen-impermeable cover can be used to begin (by removing it) or to halt the electrotransport process of the device (by re-covering the orifice).

In one embodiment, the carrier layer **120** contains at least two active agents carrying opposite electric charges. One example of such a composition is a composition containing from about 0.5 to about 2% salicylic acid and from about 0.01 to about 0.2% of a cationic quaternary ammonium antimicrobial agents (such as benzalkonium chloride, benzethonium chloride, methyl benzethonium chloride, and cetylpyridinium chloride), phenol, and/or chlorhexidine gluconate. The device **500** of the present invention can simultaneously deliver both active agents of opposite charges into the membrane.

The backing layer **160** may have some gas permeability, so called "breathable backing". The examples of such "breathable backing" material include, but are not limited to, a cotton or synthetic woven and nonwoven fabric layer,

such as those fabric materials commonly used for bandages and sports bandages.

The lighting portion of the LED **122** is preferable located in the carrier layer **120** in close proximity to the skin. Locating the light source in the carrier layer **120** affixed to the barrier membrane has an advantage of minimizing the loss of light energy from reflection of skin surface. In addition, a light reflective layer may be used as the backing layer **160** (e.g., metalized polymer film) to further enhance the efficacy of phototherapy, and to achieve more homogeneous irradiation. The backing layer **160** may optionally be perforated as certain spots to make the light visible to the user to serve as an indicator that the device is working normally.

FIG's 4 and 5 disclose one embodiment of the two different configurations of conductive electrode **140** and **240** in carrier layer **120**.

Another embodiment of the present invention is represented schematically in FIG. 6. The electrotransport device **800** containes two electrode assemblies 200 and 600, respective adhesive layers **230** and **630**, respective carrier layers **220** and **620**, respective conductive electrodes 240 and **640**, respective light emitting diodes **222** and **622**, respective housings **270** and **670**, respective electric leads **210** and **610**, battery **320** and electric switch **330**. Similar to the aforementioned typical iontophoresis device, the two electrode assemblies 200 and 600 are to be affixed to the barrier membrane with an electric insulation between them, after the release liner **100** is removed prior to use.

<u>Topical Compositions Containing Galvanic Pairs</u>

In one embodiment, the present invention features a topical composition containing a first conductive metal (such as fine flakes, wires/fibers or metal-coated fibers) selected from zinc, aluminum, copper, and their alloys; and a second conductive metal (such as fine flakes, wires/fibers or metal-coated fibers) selected from silver, copper, gold, and their alloys. Upon contact, the first conductive metal and the second conductive metal form a galvanic pair, generates electric current, and electrochemically generates ions. In a further embodiment, the difference of the standard potentials of the first conductive metal and the second conductive metal is at least about 0.1 V, such as at least about 0.5 V. For example, upon contact with a first conductive metal that contains zinc (such as fine zinc wires, zinc flakes or polymer fibers coated with zinc) and a second conductive metal that contains silver (such as a fine silver wires/fibers, silver flakes, or polymer fibers coated with silver), the composition generates electric current and zinc ions within the topical composition.

The composition may additionally contain an active agent, such as an anti-acne agent (such as salicylic acid, benzoyl peroxide, retinoic acid and/or retinol). The topical composition containing the first metal and the second metal is preferably a semi-solid dosage form (such as a gel, a hydrogel, a water-in-oil emulsion, an oil-in-water emulsion, a cream, a lotion, an ointment, a multi-emulsion, a liposome, and/or a microcapsule formulation), and may contain the aforementioned fluid suspending or fluid absorbing materials. The topical composition may be prepared as such that one of the conductive metal is formulated in a separate phase from other conductive

metal, for example, the first conductive metal (e.g., zinc flakes) is formulated in the discontinuous oil phase of an oil-in-water emulsion (e.g., a cream), while the second conductive metal (e.g., silver flakes) is formulated in the continuous aqueous phase of the emulsion. The topical composition of the present invention may also further contain a humectant (such as glycerin, propylene glycol, polyethylene glycol, sorbitol and/or urea) and aforementioned electrolytes to maintain certain moisture level and conductivity of the skin.

In one embodiment, during storage of such a topical composition, the first conductive metal and the second conduct metal are suspended substantially apart in a semi-solid composition (e.g., not usually are not in contact with each other). Upon application to the membrane (such as the skin or mucosa) and drying-out of the liquid carrier, the overlay of the first conductive metal and the second conductive metals results in galvanic couple formation and generation of electric current and metal ions of the first conductive metal, which may provide benefits to the membrane such as antimicrobial, anti-inflammation, wound healing, iontophoretic delivery of active agents, tissue stimulation, and/or sebum reduction.

In one embodiment, the wires/fibers, flakes of conductive metals, or polymer fibers coated with the conductive metals are fine enough that they can be suspended in the semi-solid compositions during storage. In a further embodiment, they are in elongated shapes. The advantages of elongated shapes of the conductive metals (e.g., fine wires/fibers, flakes and polymer fibers coated with the conductive metals) include a lower apparent density and, therefore, a better floating/suspending

capability in the topical composition; a higher probability of connected with each other when low concentrations of the conductive metals are used; and a wider and deeper range of the membrane tissue (e.g., the skin) that the galvanic current travels through and provides the benefits to.

<u>Example 1: Carriers</u>

Examples of several carriers, including the weight percentage range of the ingredients of such carriers, are set forth in Table 1.

Table 1

Component	Percent by Weight of the Carrier					
	No. 1	No. 2	No. 3	No. 4	No. 5	No. 6
Salicylic acid	0.1-10	2	2	0	0	0.1-10
Benzyl peroxide	0	0	0	0.5-10	0	0
Sulfur	0	0	0	0	3	3
Resorcinol	0	0	0	1	1	1
Benzalkonium chloride	0-2	0.1	0.1	0-2	0-2	0-2
Benzethonium or methylbezethonium chloride	0-2	0	0	0-2	0-2	0-2
Cetylpyridium chloride	0-2	0.1	0.1	0-2	0-2	0-2
Phospholipid CDM	0-40	5	5	0-40	0-40	0-40
Hydrogen peroxide	0-30	0	3	0-30	0-30	0-30
Buffer (citrate, lactate, or phosphate salts of sodium, potassium, or lithium	0-10	2	2	0-10	0-10	0-10
Gelling agent (e.g., polyacrylates, cellulose, natural or	0-20	5	5	0-20	0-20	0-20

synthetic gums, or polyacrylamide)						
Chelating agent (e.g., EDTA)	0-2	0.1	0.1	0-2	0-2	0-2
Propylene glycol	0-30	20	15	0-30	0-30	0-30
Polyethylene glycol	0-50	0	0	0-50	0-50	0-50
Polypropylene glycol	0-40	0	0	0-40	0-40	0-40
Ethyl alcohol	0-50	0	15	0-50	0-50	0-50
Isopropyl alcohol	0-50	0	0	0-50	0-50	0-50
Dimethyl isosorbide	0-20	2	0	0-20	0-20	0-20
Isopropyl myristate	0-30	1	1	0-30	0-30	0-30
Purified water	Qs to 100	Qs to 100	Qs to 100	Qs to 100	Qs to 100	Qs to 100

In order to evaluate the proposed mechanism of action for the electrochemically generated beneficial agents, an *in vitro* microbiologic study was conducted to investigate effect of electrolysis on *P. acne* inhibition in certain electrochemical systems; and an *in vivo* study was conducted in human volunteers using a commercial iontophoresis device.

EXAMPLE 2. *In vitro* Inhibition of *P. acnes* by Electrolysis

A BacT/ALERT system (BioMerieux, Inc., Durham, NC) was used in the *P. acnes* inhibition experiment. Briefly, 40 ml of an anaerobic casein and soy based broth culture medium in a bottle (BacT/ALERT SN, Organon Tekniks Corp., Durham, NC) was inoculated with *P. acnes*. The fully automated BacT/ALERT system was used to detect *P. acnes* growth over a 14-day study at 35°C by continuous monitoring of CO_2 production using an optical colorimetric sensory system.

A selected pair of the electrodes (Table 2, Columns 2 and 3) was disinfected with 70% isopropyl alcohol, and inserted through the rubber stopper into the culture medium in a nitrogen glove box. Some electrodes were connected to the poles of a battery (either 1.5 or 3V as indicated in Table 2, Column 3) for 30 minutes. The electrodes were then immediately removed from the BacT/ALERT bottle, which was then placed into the automated incubation and monitoring system for two weeks. Other elecrodes (i.e., Nos. 3 & 5 in Table 2), were not connected to an external battery, but rather were directly connected to each other at their ends outside the BacT/ALERT bottle to form galvanic couple. The electrodes of these galvanic couples (i.e., Nos. 3 & 5) remained in contact with the culture medium in the bottle during the 14-day study.

Zinc as the positive electrode (anode), with various materials as the negative electrode (cathode), was evaluated through the test conditions 1 to 7 (No.1-7 in Column 1). Column 4 shows the voltage applied to the conductive electrode by the external battery. However, by simply connecting two conductive electrode materials, a voltage was also generated just from the galvanic pair. For example, zinc-silver/silver chloride galvanic couple has a voltage of 0.9849V or about 1V ($Zn^{2+} + 2e^- = Zn$, standard potential: -0.7626V, and $AgCl + e^- = Ag + Cl^-$, standard potential: 0.2223V) and zinc-copper galvanic couple has a voltage of about 1.1-1.3V ($Cu^{2+} + 2e^- = Cu$, standard potential: 0.340V, and $Cu+ + e^- = Cu$, standard potential: 0.520V) Reference: Electrochemistry Handbook, 1995, Table 14.1, McGraw-Hill, Inc. New York, NY).

In the test condition No. 7, the electrodes (i.e., zinc-silver/silver chloride galvanic couple) were taken from a commercial iontophoresis device (IontoPatch, SP, Birch Point Medical, Inc., Oakdale, MN). The IontoPatch is an iontophoresis device powered by a galvanic couple "battery strip" made of zinc and silver/silver chloride in a bandage-like device. In this experiment, the "battery strip" in the IontoPatch was taken out of the bandage-like device, and placed into the BacT/ALERT bottle. The electrodes of the commercial zinc-silver/silver chloride galvanic couple (No. 7) remained in the BacT/ALERT bottle through out the entire two-week experiments. Test conditions of Nos. 15-17 were positive controls (i.e., without electrodes): Test condition No. 15 used a concentrated *P. acne* culture that was used to inoculate the rest of the culture medium in each BacT/ALERT bottle to *P. acnes* counts of 10^6 per ml and Test conditions No. 16 and No. 17 used the inoculated culture medium of *P. acnes* counts of 10^6 per ml (with the rubber stoppers of No. 16 additionally being punctured in a way similar to the rest of electrode-tested conditions in order to eliminate any false *P. acnes* inhibition results due to potential environmental oxygen entry into the test bottle and affecting anaerobic *P. acnes* growth).

TABLE 2

No.	Positive Electrode	Negative Electrode	Voltage applied by connected to a battery or batteries	Average time to Positive *P. acnes* Growth (days)	Number positive/ number tested
1	Zinc	Silver/Silver Chloride	3V	-	0/3
2	Zinc	Zinc	3V	-	0/1
3	Zinc	Copper	None[a]	-	0/2
4	Zinc	Copper	1.5V	-	0/1
5	Zinc	Silver/Silver Chloride	None[a]	-	0/2
6	Zinc	Silver/Silver Chloride	1.5V	-	0/2
7	Zinc	Silver/Silver Chloride	None[a]	-[b]	2/6
8	Copper	Silver/Silver Chloride	3V	-	0/3
9	Copper	Copper	3V	-	0/2
10	Platinum	Silver/Silver Chloride	3V	1.6	2/2
11	Platinum	Platinum	3V	1.1	1/1
12	Silver	Silver/Silver Chloride	3V	5.7[c]	2/3
13	Silver	Silver	3V	2.8d	2/2

14	Silver/Silver Chloride	Silver/Silver Chloride	3V	3.0	2/2
15	None	None	None	0.8	2/2
16	None	None	None	1.4	2/2
17	None	None	None	1.3	2/2

a. The conductive metal electrodes were not connected to any battery, but to each other. Therefore, there is a voltage across the two electrode dictated by the galvanic pair.

b. A total of 6 samples were tested; 4 negative and 2 positive (0.6d & 0.8d); the positive ones were very likely due to bacterial contamination since they were detected faster then the positive control samples (Nos. 16 & 17), and therefore were omitted.

c. Out of 3 samples, two positive (4.1d & 7.3d) were averaged

The zinc anode was surprisingly found to almost completely inhibit *P. acne* growth during the 14-day incubation study at the all of the voltage conditions tested (Nos. 1-7; in No. 7, two of the six commercial galvanic couples showed positive *P. acnes* growth probably due bacterial contamination, see Note C of Table 2). The copper anode was also found to significantly inhibit *P acnes* growth(Nos. 8-9). Under these experimental conditions, the platinum anode showed little *P. acne* inhibition effect and the silver or silver/silver chloride anodes provided only a weak *P. acne* inhibition. Since all the positive control conditions (Nos. 15-17) showed positive P. acnes growth less than two days after the beginning of the

study, the negative *P. acnes* growth can be attributed to the inhibition effect of the electrochemically generated species or electric current passage through the culture medium. Because electric current passage in Nos. 10-14 failed to show strong *P. acnes* inhibition as those in Nos. 1-9, the observed bacterial inhibition in Nos. 1-9 were likely due to certain electrochemical reactions occurred at the anode, namely, when zinc and copper were used as the anode. It was also unexpected that the silver ions released from silver or silver/silver chloride anode under these experimental conditions failed to show the same *P. acnes* inhibition (Nos. 12-14), since silver ion is well-known anti-microbial agent. See. e.g., Spacciapoli et al. ("*Antimicrobial activity of silver nitrate against periodontal pathogens.*", J Periodontal Res 36: 2, 108-13, Apr, 2001). It was surprising that, in the absence of external battery (Nos. 3, 5 and 7), a pair of electrodes of galvanic couple with zinc as anode were sufficient to inhibit *P. acnes* growth during the entire two week study.

EXAMPLE 3. *In vitro* Electrode-salicylic acid compatibility

The following experiment was conducted to determine the compatibility of electrodes with salicylic acid. A pair of test electrodes was immersed in 5 ml of 1.5% salicylic acid solution (solvent 50% ethanol/ 50% water). A pre-determined voltage was applied to the electrodes (by connecting the electrodes to a battery or batteries) for certain length of time as indicated in Table 3. Observations were made on color change of the test solution.

The solution with the zinc anode showed no discoloration, indicating good compatibility with

salicylic acid during the passage of electric current. Use of the platinum anode unexpectedly resulted in discoloration, indicating incompatibility with salicylic acid under this experimental condition.

Table 3

Electrode Material		Voltage (V)	Test Duration (min)	Observation
Anode (+)	Cathode (-)			Solution color change
Platinum	Platinum	3	10	Colorless → yellow
Platinum	Platinum	9	10	Colorless → brown
Zinc	Platinum	1.5	10	No color change
Zinc	Platinum	3	10	No color change
Zinc	Platinum	9	30	No color change

EXAMPLE 4: In vivo human iontophoresis study

An *in vivo* study was conducted in human volunteers using a commercial iontophoresis device (IontoPatch®, Model: SP, Birch Point Medical Inc., North Oakdale, MN). The study recruited the healthy female volunteers with oily skin, aged from 20-45 years. The sebumeter reading from each subject's forehead was at least greater than 150 $mg/cm^2/hr$. The study was blind and controlled. Briefly, an IontoPatch® with a voltage of 1 volt, an operating current of 0.06 mA, and an active treatment area of 1.25 in^2, was applied to the treatment site of the human subject (e.g. forehead). The positive electrode and negative consisted of zinc and silver/silver chloride (Ag/AgCl)material, respectively. Both electrodes were

filled with saline (0.9% NaCl). As soon as the saline solution was added into the different electrodes, the electric patch begin to function. The patch was left on the treatment area overnight (e.g., approximately 8 hours).

The following evaluations were conducted: (i) the effects of electrolysis on the skin condition were monitored using a normal photography and (ii) The change in *p. acnes* counts was determined through analyzing the cup wash solution for the treatment site before and after wearing the patch overnight.The cup wash micro sampling procedure was performed as follows: a cylindrical cup (2.1 cm diameter and 2.5 cm height) having two open ends was fastened onto the treatment area. The treatment area inside the cylinder was then washed with 2 ml of cleansing buffer (sterile 0.075M Phosphate Buffer containing 0.1% Triton X-100) while the same area with a sterile polished glass. The wash solution was then collected. This washing procedure was then repeated. The two collected samples were pooled and used in the *P-acnes* analysis.

The *P. acnes* counts were determined by Spiral Plating the scrub samples anaerobically in Actinomyces Agar for 5 days, and the predominant contaminants on the spiral plates were Gram stained and identified using the VITEK System. Using an automated colony counter, the P-acne count per mL of each sample buffer was determined.

After only one overnight patch application, *P. acne* quantification measurement on the treatment area shows a 45% P. acne reduction relative to the baseline under the zinc anode and 30% under the Ag/AgCl cathode. After four consecutive overnight patch applications, photo images displayed the clear evidences of significant reduction in

the color and size of post-acne hyperpigmentation spot under the zinc electrode. This test subject had a post-acne hyperpigmentation spot at the test skin site. The appearance of the hyperpigmented spot was improved from a very dark color to a lighter color.

Also, after four consecutive overnight patch applications, photo images also displayed the evidence of significant reduction in the color and size of an acne pimple under the Ag/AgCl electrode. This test subject had an acne pimple at the test skin site. The redness of the pimple was reduced from very red color to become almost invisible.

It is understood that while the invention has been described in conjunction with the detailed description thereof, that the foregoing description is intended to illustrate and not limit the scope of the invention, which is defined by the scope of the appended claims. Other aspects, advantages, and modifications are within the claims.

What is claimed is: